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Review

Revascularization of Immature and Mature Teeth with Necrotic Pulp

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Abstract

Revascularization is a regenerative endodontic procedure that focuses on revitalizing necrotic pulp tissue, offering significant advantages over traditional treatments such as apexification or root canal therapy. Immature teeth with open apices exhibit favorable conditions for revascularization, allowing for continued root development, dentinal wall thickening, and apical closure. This is facilitated by the presence of stem cells, growth factors, and an adequate scaffold, such as a blood clot, which supports cellular migration and tissue regeneration. Mature teeth, characterized by closed apices, present unique challenges due to limited regenerative capacity and restricted vascular access. Despite these limitations, the use of bioactive scaffolds, platelet concentrates, and advanced disinfection techniques has demonstrated potential in achieving partial regeneration and periapical healing. The success of revascularization depends on multiple factors, including microbial control, scaffold stability, the quality of coronal sealing, and patient-specific variables such as age and systemic health. Effective irrigation with agents like sodium hypochlorite and ethylenediaminetetraacetic acid (EDTA), combined with intracanal medicaments such as triple antibiotic paste, plays a critical role in reducing microbial load while maintaining cellular viability. Radiographic evaluations often reveal notable differences between immature and mature teeth, with the former showing more consistent structural improvements, such as root elongation and thickened dentinal walls, compared to the latter. Emerging strategies involving biomaterials, injectable scaffolds, and platelet-rich fibrin are advancing the predictability of outcomes, particularly for mature teeth. However, variability in clinical results, coupled with challenges in achieving true pulp-dentin regeneration, underscores the need for further research and innovation. Revascularization continues to evolve as a promising therapeutic approach, leveraging biological principles to optimize outcomes for patients with necrotic pulp in both immature and mature teeth.

Keywords: *Revascularization, necrotic pulp, regenerative endodontics, immature teeth, mature teeth*

Introduction

Revascularization is a biologically driven treatment aimed at revitalizing necrotic pulp tissue in immature and mature teeth, offering an alternative to traditional apexification and root canal therapy. This regenerative endodontic procedure leverages the potential of stem cells, scaffold materials, and signaling molecules to restore the pulp-dentin complex, enhance root development, and maintain long-term tooth viability. The principle behind revascularization is to create a conducive environment for cellular proliferation and vascular in-growth, thereby reestablishing a functional pulp tissue capable of regenerating dentin (1).

Necrotic pulp in immature teeth often results from dental trauma or extensive carious lesions, halting root development and compromising the structural integrity of the tooth. These conditions present unique challenges, as conventional endodontic procedures may fail to provide long-term solutions for immature teeth with open apices. Revascularization, however, has shown promising results in inducing continued root maturation and apical closure, fostering improved prognosis for such teeth (2). On the other hand, revascularization of mature teeth with necrotic pulp represents a more complex scenario due to their closed apical anatomy and reduced regenerative potential. Nonetheless, advancements in regenerative techniques and materials have expanded the scope of revascularization to include mature teeth under specific conditions.

The success of revascularization depends on several critical factors, including the eradication of microbial contamination, induction of controlled bleeding to create a fibrin scaffold, and appropriate sealing of the coronal restoration. The role of antimicrobial agents, biocompatible scaffolds, and growth factors in optimizing the microenvironment for regeneration has been extensively studied. Furthermore, emerging evidence highlights the significance of the host's regenerative capacity, age, and the condition of the periapical tissues in determining treatment outcomes (3). Although revascularization holds significant potential, challenges persist. Inconsistent clinical outcomes, variability in case selection criteria, and the lack of standardized protocols limit its widespread adoption. In particular, achieving predictable results in mature teeth remains an area of active research and innovation. The histological nature of the regenerated tissue—often reported as a mix of fibrous tissue and mineralized components rather than true pulp tissue—also raises questions about the quality of regeneration achieved (4).

As regenerative endodontics continues to evolve, there is a growing emphasis on understanding the biological mechanisms underlying revascularization and refining clinical techniques to enhance outcomes. The integration of advanced biomaterials, innovative delivery systems, and precision diagnostics offers new avenues for improving the efficacy and predictability of this treatment modality. By bridging the gap between experimental research and clinical practice, revascularization has the potential to revolutionize the management of necrotic pulp in both immature and mature teeth.

Review

Revascularization has emerged as a groundbreaking approach in managing necrotic pulp, particularly in immature teeth, where traditional therapies like apexification fall short in promoting root development. The biological mechanism relies on the interaction between stem cells, scaffold materials, and signaling molecules to stimulate regeneration of the pulp-dentin complex. Controlled bleeding induced during revascularization procedures serves as a natural scaffold, providing an environment conducive to cellular infiltration and differentiation (5). The success of this process in immature teeth is largely attributed to the presence of open apices, which facilitate the ingress of stem cells and growth factors essential for regeneration.

However, the application of revascularization in mature teeth poses significant challenges due to the presence of closed apices and reduced vascular access. Advances in biomaterials, such as bioactive scaffolds and the incorporation of platelet-rich plasma, have shown promise in overcoming these

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limitations by creating a microenvironment that mimics natural tissue regeneration (6). Despite these advancements, variability in clinical outcomes remains a concern, often influenced by patient-specific factors, including age and the condition of periapical tissues. Furthermore, histological analyses frequently reveal regenerated tissues comprising fibrous and bone-like components rather than functional pulp, indicating the need for further refinement of techniques to achieve true pulp regeneration.

Biological Basis of Revascularization in Immature and Mature Teeth

The biological foundation of revascularization lies in leveraging the regenerative potential of stem cells, growth factors, and the body's inherent healing mechanisms. This process begins with disinfection protocols aimed at eliminating microbial contamination from the root canal, followed by induction of controlled bleeding into the canal space. The resulting blood clot serves as a scaffold, enabling the migration and differentiation of stem cells that originate primarily from the apical papilla in immature teeth (7). These stem cells, known as stem cells of the apical papilla (SCAP), are pivotal due to their high proliferative capacity and ability to differentiate into odontoblast-like cells that contribute to dentin-pulp complex regeneration.

Immature teeth with open apices present an ideal environment for revascularization. The wider apical foramen allows for easier ingress of progenitor cells and vascular components from the surrounding periapical tissues (8). Additionally, the availability of growth factors, such as bone morphogenetic proteins and vascular endothelial growth factor, further enhances cellular activity and angiogenesis, ensuring the formation of new vascular networks. These vascular structures are critical for delivering nutrients and signaling molecules necessary for cellular survival and tissue development. In contrast, the biological potential for revascularization in mature teeth with necrotic pulp is considerably more limited due to the presence of closed apices and the diminished availability of SCAP. The lack of apical openings restricts the entry of regenerative cells, creating a challenging environment for effective tissue regeneration (9). To address this limitation, novel therapeutic approaches have been explored. These include the use of platelet-rich fibrin (PRF) and injectable scaffolds infused with bioactive molecules. PRF, in particular, has shown promise in enhancing the regenerative process by releasing growth factors over an extended period, promoting cell migration and proliferation.

An integral aspect of revascularization is the interaction between the scaffold and surrounding cellular components. The blood clot that forms in the canal space acts as a provisional scaffold, providing structural support for cellular attachment and migration. However, studies have highlighted inconsistencies in the composition and stability of the clot, particularly in mature teeth (10). This variability has prompted interest in synthetic and natural scaffolds, such as hydrogels and collagen-based matrices, which offer better control over the microenvironment. These materials not only enhance the recruitment of stem cells but also provide a more stable framework for tissue formation.

The biological basis of revascularization is also influenced by the host immune response. The inflammatory milieu within the root canal plays a dual role: while low levels of inflammation can stimulate regeneration, excessive inflammation can impede the process (11). Understanding and modulating this inflammatory response is crucial, particularly in cases of mature teeth, where the healing potential is inherently compromised. Research into the role of macrophages and cytokines in regulating the balance between inflammation and regeneration continues to shed light on optimizing outcomes in such cases. While substantial progress has been made in elucidating the biological mechanisms underlying revascularization, there remain critical gaps in understanding, particularly regarding the variability in tissue outcomes. Histological analyses often reveal the formation of fibrous tissue or cementum-like structures instead of true pulp-dentin regeneration. Further studies are essential to refine

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existing protocols and explore adjunctive therapies that can maximize the regenerative capacity in both immature and mature teeth.

Clinical Protocols and Techniques for Revascularization

The clinical implementation of revascularization involves a meticulous sequence of steps aimed at creating an optimal environment for tissue regeneration. The process begins with disinfection of the root canal system, typically achieved through the use of irrigants like sodium hypochlorite and ethylenediaminetetraacetic acid (EDTA). Sodium hypochlorite effectively eliminates microbial contamination while EDTA facilitates the release of growth factors from the dentin matrix, which are crucial for initiating regenerative processes (12). This step is particularly significant, as residual microbial biofilms can compromise the outcomes of revascularization by inducing inflammation and impeding tissue formation. Following disinfection, the induction of controlled bleeding into the root canal is a cornerstone of revascularization. This step is performed using endodontic files to irritate the apical tissues, stimulating bleeding that leads to the formation of a blood clot within the canal space. This clot serves as a natural scaffold, providing structural support and releasing signaling molecules that attract stem cells and promote angiogenesis (13). The technique requires careful execution to avoid over-bleeding or damage to periapical tissues, as both can complicate the healing process. Achieving an appropriate level of hemostasis is critical for stabilizing the clot and ensuring it remains intact throughout the regeneration phase.

The role of intracanal medicaments, such as triple antibiotic paste (TAP) or calcium hydroxide, is another important component of the protocol. TAP, a combination of ciprofloxacin, metronidazole, and minocycline, is widely used for its broad-spectrum antimicrobial activity and ability to reduce microbial load in the canal system. However, concerns regarding the discoloration caused by minocycline have led to modifications in its formulation, with alternative combinations such as double antibiotic paste being explored (14). Calcium hydroxide is another popular choice due to its ability to maintain an alkaline pH and promote the release of bioactive molecules. The selection of medicaments depends on the specific clinical scenario and the clinician's preference, as both options have demonstrated success in various studies.

Coronal sealing of the canal system with a biocompatible material is essential to prevent microbial reinfection and preserve the integrity of the regenerated tissues. Materials such as mineral trioxide aggregate (MTA) or biodentine are commonly used for their excellent sealing properties and ability to support tissue regeneration. These materials are applied as a final restoration after the induction of bleeding and stabilization of the scaffold. The selection of coronal restorations, including composite resins or glass ionomer cements, further enhances the long-term success of the procedure by protecting the tooth from structural compromise and bacterial ingress (15).

Innovations in the clinical protocols for revascularization have introduced the use of platelet concentrates, such as PRF and platelet-rich plasma (PRP), as adjuncts to enhance the regenerative potential (16). These concentrates are rich in growth factors, including platelet-derived growth factor (PDGF) and transforming growth factor-beta (TGF-β), which promote cellular proliferation, differentiation, and vascularization. By incorporating PRF or PRP into the canal space, clinicians aim to augment the biological foundation of revascularization and achieve more consistent outcomes, particularly in challenging cases involving mature teeth or compromised apical conditions.

The clinical techniques employed in revascularization continue to evolve as new materials and methods are developed. Advances in imaging technologies, such as cone-beam computed tomography (CBCT), have enhanced the ability to assess periapical healing and root development post-treatment. Additionally, the integration of bioactive scaffolds, injectable hydrogels, and gene therapy into clinical practice offers exciting

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possibilities for the future of regenerative endodontics.

Factors Influencing Success Rates in Revascularization

The success of revascularization procedures is contingent upon a myriad of interrelated factors, ranging from patient-specific characteristics to procedural techniques. Patient age is one of the most critical determinants, as younger patients tend to exhibit higher success rates due to the greater regenerative potential of stem cells in the apical papilla and more robust vascular networks in developing teeth. The viability of stem cells diminishes with age, reducing the likelihood of achieving pulp regeneration in older individuals (17). This underscores the importance of early intervention in cases of necrotic pulp, particularly in immature teeth, to harness their inherent regenerative capabilities.

Microbial control within the root canal system plays an equally pivotal role in the success of revascularization. The presence of residual bacterial biofilms can trigger persistent inflammation, impeding the regenerative process and leading to treatment failure. The choice of irrigants and intracanal medicaments directly influences microbial eradication. Sodium hypochlorite and EDTA are commonly used to achieve disinfection, while their concentrations and duration of application must be carefully calibrated to avoid cytotoxic effects on stem cells (18). Furthermore, the biocompatibility of medicaments such as triple antibiotic paste and calcium hydroxide is critical, as overly aggressive formulations can compromise cellular viability and delay tissue formation.

The condition of the periapical tissues also significantly impacts the outcomes of revascularization. Healthy periapical tissues provide a reservoir of stem cells, growth factors, and vascular components necessary for regeneration. In contrast, extensive periapical pathology can limit the availability of these essential elements, reducing the likelihood of successful tissue repair. Effective management of periapical inflammation through pre-treatment with antimicrobial agents or additional disinfection steps is often required in such cases to create a conducive environment for regeneration (19, 20). The controlled bleeding step, achieved by irritating the periapical tissues with endodontic files, ensures the formation of a blood clot that acts as a natural scaffold for cellular migration and differentiation. However, excessive bleeding or clot instability can disrupt the regenerative process, leading to inconsistent outcomes. Techniques to optimize clot formation, including the use of hemostatic agents and the careful adjustment of canal instrumentation, are crucial for maintaining the structural integrity of the scaffold throughout the healing process.

The type of coronal restoration and the quality of the seal provided also play an essential role in determining long-term success. Leakage through coronal restorations can allow microbial reinfection, jeopardizing the regeneration process. Materials such as MTA and biodentine have been shown to provide superior sealing properties, reducing the risk of reinfection and ensuring a sterile environment conducive to tissue regeneration (21). Additionally, these materials support the attachment of newly formed tissues, further enhancing treatment outcomes.

Emerging evidence also highlights the importance of individual genetic predisposition in influencing the success of revascularization. Variations in the expression of genes involved in stem cell differentiation, angiogenesis, and immune response can affect a patient's capacity for tissue regeneration. Although the clinical application of genetic screening in revascularization is still in its infancy, this area holds significant potential for identifying patients who are most likely to benefit from the procedure and tailoring treatment protocols accordingly.

Comparative Outcomes: Immature vs. Mature Teeth

The clinical outcomes of revascularization vary significantly between immature and mature teeth due to differences in anatomical and biological factors. Immature teeth, characterized by open apices and less rigid dentinal walls, provide a

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favorable environment for the ingress of regenerative cells and vascular components. These teeth often show continued root development, including thickening of dentinal walls and apical closure, as a direct response to revascularization (22). This regenerative response is attributed to the presence of SCAP and the availability of growth factors from periapical tissues. Such features enable immature teeth to achieve near-complete structural and functional restoration.

In contrast, mature teeth with necrotic pulp present unique challenges due to the closure of apices and reduced regenerative capacity. The limited entry of vascular and cellular elements into the canal system makes regeneration more difficult. Clinical studies have shown that mature teeth undergoing revascularization often form fibrous or cementum-like tissues rather than true pulp-dentin complexes (23). While some degree of healing is achieved, the outcomes are typically less predictable compared to immature teeth. This discrepancy underscores the importance of anatomical differences in determining the success of regenerative endodontic therapies. A critical factor influencing the outcomes in both tooth types is the ability to establish a stable scaffold for cellular attachment and tissue formation. The formation of a blood clot in immature teeth is often more consistent due to the larger apical opening, which facilitates the influx of blood and regenerative cells. In mature teeth, achieving and maintaining an adequate scaffold can be more challenging, leading to variable clinical results (24). The use of synthetic or bioengineered scaffolds, such as hydrogels and bioactive matrices, has shown potential in overcoming these limitations, particularly for mature teeth.

Radiographic assessment of post-treatment outcomes also reveals stark differences between the two groups. In immature teeth, evidence of continued root elongation and thickening of dentinal walls is commonly observed, indicating successful tissue regeneration. In mature teeth, the radiographic changes are often confined to periapical healing, with minimal or no signs of structural changes in the root. This disparity is largely due to the reduced ability of mature teeth to stimulate and sustain odontoblastic differentiation and matrix deposition, even when regenerative protocols are meticulously followed (25). Additionally, patient-specific factors, such as age and immune response, play a crucial role in comparative outcomes. Younger patients with immature teeth exhibit a more robust regenerative potential, which is less influenced by systemic conditions. Conversely, mature teeth in older patients are more likely to be affected by systemic factors such as diabetes or immune dysfunction, which can impair healing and regeneration. These variations highlight the need for tailored approaches to revascularization based on the maturity of the tooth and the overall health status of the patient.

Conclusion

Revascularization represents a transformative approach in regenerative endodontics, offering promising outcomes for immature teeth and expanding the potential for managing mature teeth under select conditions. While immature teeth benefit from their anatomical advantages, advancements in materials and techniques are gradually bridging the gap for mature teeth. The variability in clinical results highlights the need for continued research to refine protocols and enhance predictability. By integrating biological insights with innovative clinical strategies, revascularization has the potential to redefine the future of endodontic therapy.

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Conflict of interest

There is no conflict of interest

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Data availability

Data that support the findings of this study are embedded within the manuscript.

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Author contribution

All authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

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